

RISK FACTORS FOR RESPIRATORY FAILURE FOLLOWING OPERATIVE STABILIZATION OF THORACIC AND LUMBAR SPINE FRACTURES

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Background: Respiratory failure is a serious complication that can adversely affect the hospital course and survival of multiply injured patients. Some studies have suggested that delayed surgical stabilization of spine fractures may increase the incidence of respiratory complications. However, the authors of these studies analyzed small sets of patients and did not assess the independent effects of multiple risk factors.

Methods: A retrospective cohort study was conducted at a regional level-I trauma center to identify risk factors for respiratory failure in patients with surgically treated thoracic and lumbar spine fractures. Demographic, diagnostic, and procedural variables were identified. The incidence of respiratory failure was determined in an adult respiratory distress syndrome registry maintained concurrently at the same institution. Univariate and multivariate analyses were used to determine independent risk factors for respiratory failure. An algorithm was formulated to predict respiratory failure.

Results: Respiratory failure developed in 140 of the 1032 patients in the study cohort. Patients with respiratory failure were older; had a higher mean Injury Severity Score (ISS) and Charlson Comorbidity Index Score; had greater incidences of pneumothorax, pulmonary contusion, and thoracic level injury; had a lower mean Glasgow Coma Score (GCS); were more likely to have had a posterior surgical approach; and had a longer mean time from admission to surgical stabilization than the patients without respiratory failure ($p < 0.05$). Multivariate analysis identified five independent risk factors for respiratory failure: an age of more than thirty-five years, an ISS of >25 points, a GCS of ≤ 12 points, blunt chest injury, and surgical stabilization performed more than two days after admission. An algorithm was created to determine, on the basis of the number of preoperative predictors present, the relative risk of respiratory failure when surgery was delayed for more than two days.

Conclusions: Independent risk factors for respiratory failure were identified in an analysis of a large cohort of patients who had undergone operative stabilization of thoracic and lumbar spine fractures. Early operative stabilization of these fractures, the only risk factor that can be controlled by the physician, may decrease the risk of respiratory failure in multiply injured patients.

Level of Evidence: Prognostic Level II. See Instructions to Authors for a complete description of levels of evidence.

Early operative stabilization of spinal fractures in multiply injured patients is advocated on the basis of the belief that it reduces complications associated with prolonged recumbency. Evidence supporting this view was reported by Schlegel et al. in a retrospective analysis of 138 patients who had undergone operative fixation of unstable spinal fractures¹. They found that, of ninety-eight patients with thoracic and lumbar fractures, those who had an Injury Severity Scores (ISS) of ≥ 18 points and had had surgery more than seventy-two hours after admission had significantly greater collective morbidity ($p < 0.05$). Unfortunately, because

of the small number of patients in the study, the significance of the effect of surgical timing on the rates of individual morbid conditions such as pulmonary complications, urinary tract infections, and thromboembolic disease could not be determined. Furthermore, the impact of other injuries, such as those of the chest and head, was not considered.

Croce et al. subsequently presented additional supportive evidence in an analysis of 291 patients with spinal column injuries who underwent surgical fixation². Several variables were recorded, including age, ISS, Glasgow Coma Score (GCS), blood transfusion requirements, chest Abbreviated Injury Scale (AIS)

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severity score, neurological injury, and level of spinal injury. Individuals who had undergone operative fixation within three days after the injury had a significantly lower incidence of pneumonia ($p = 0.03$) and a shorter stay in the intensive care unit ($p = 0.001$). Subgroup analysis of patients with thoracic spine fractures demonstrated that those who had undergone surgical fixation less than three days after the injury had a lower incidence of pneumonia and fewer days of ventilator use, in the intensive care unit, and in the hospital compared with patients who had undergone surgical fixation more than three days after the injury. Statistical analysis consisted of multiple univariate comparisons between patients grouped by injury characteristics. Multivariate analysis was not done.

Kerwin et al.³ recently performed a similar analysis of 299 patients with spinal column fractures requiring surgical stabilization. They carried out univariate analysis to compare patients who had undergone surgical stabilization within seventy-two hours after the injury with those for whom stabilization had been delayed for more than seventy-two hours. Again, multivariate analysis was not done. The group with the early surgery was found to have a shorter length of hospital stay. No difference in the incidence of pneumonia or mortality could be demonstrated between the two groups. Subgroup analysis of the patients with thoracic spine injuries and associated spinal cord injury showed the incidence of pneumonia to be lower when surgery had been performed within seventy-two hours after the injury. The authors concluded that a rigid protocol to determine the timing of surgical fixation is not justified and treatment should be individualized to the medical condition of each patient.

The authors of the above studies explored the premise that early stabilization of spinal fractures improves non-neurological outcomes, but the studies lacked sufficient numbers of patients to allow a more rigorous statistical analysis. It is clear that many variables contribute to the outcomes in severely injured patients, and it would be difficult, if not impossible, to address all of these variables in any study. Nevertheless, an analysis relative to a discrete, categorical outcome variable in a larger cohort of patients would be useful for determining whether early surgical stabilization of unstable spinal fractures is advisable.

Our institution is a regional trauma center that serves as the only level-I trauma center for five northwestern states. The institution has more than 5000 annual trauma admissions, including a large number of patients with thoracic and lumbar spine fractures that are treated with surgical stabilization. Data on all trauma admissions since 1985 have been entered into the institutional trauma registry. Patients in whom an acute lung injury or adult respiratory distress syndrome develops are independently entered into a separate adult respiratory distress syndrome registry that has been maintained over the same time-period. It was therefore possible to identify a large number of patients who had undergone surgical stabilization of thoracolumbar fractures as well as the proportion in whom respiratory failure developed as a result of acute lung injury or adult respiratory distress syndrome. Identification of this large cohort of patients enabled us to perform more rigorous statistical anal-

ysis than had been done by previous investigators. Specifically, it allowed use of multivariate analysis to identify independent risk factors for the development of acute lung injury or adult respiratory distress syndrome. Our hypothesis was that the time to surgery is an independent risk factor for the development of respiratory failure in trauma patients undergoing surgical stabilization of thoracic and lumbar fractures.

Materials and Methods

A study proposal was submitted and approval was obtained from the human subjects division at our institution before the study began. The integrity of the database and patient confidentiality were maintained according to the United States Health Insurance Portability and Accountability Act (HIPAA) regulations and the policies of our institution. Data were obtained from the institutional trauma registry and adult respiratory distress syndrome registry. Our trauma registry is a computerized database that contains information on all patients evaluated for traumatic injury at our institution who either were admitted to the hospital or died in the emergency department. The registry is used for quality improvement and clinical research, and it provides data to the Washington State Trauma Registry⁴. The adult respiratory distress syndrome registry at our institution is a prospectively collected research database that is part of an ongoing Adult Respiratory Distress Syndrome Specialized Center of Research program at our institution. All patients in the intensive care unit were evaluated daily to identify those with acute lung injury or adult respiratory distress syndrome for entry into the database⁵.

The trauma registry was queried to identify all patients who had been treated for thoracic and lumbar spine fractures from January 1985 through January 2004. Demographic, procedural, and outcome variables were obtained in separate Microsoft Excel spreadsheets (Microsoft, Redmond, Washington). The demographic variables that were collected included age; ISS; AIS scores for the head and neck, face, chest, abdomen, extremities, and external; GCS on initial evaluation in the emergency department; comorbidities; smoking history; and diagnostic codes (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM]) for spinal injury, pulmonary contusion, and pneumothorax. The procedural variables included the date and time of admission to the emergency department, the procedure code (ICD-9-CM) for the surgical stabilization of the spine, and the date and time of the spine surgery. The time to surgery was calculated in hours and was converted to a hospital day for data analysis, so that surgery done from zero to twenty-four hours after admission was designated as having been performed on day 1, surgery done from twenty-five to forty-eight hours after admission was designated as having been performed on day 2, and so on. The outcome variables were the duration of the stay in the intensive care unit, the duration of hospitalization, and mortality. The spreadsheets were examined for duplicate and missing entries. Duplicate entries were rectified, and patients with missing entries were excluded. We then queried the adult respiratory distress syndrome registry to search for the

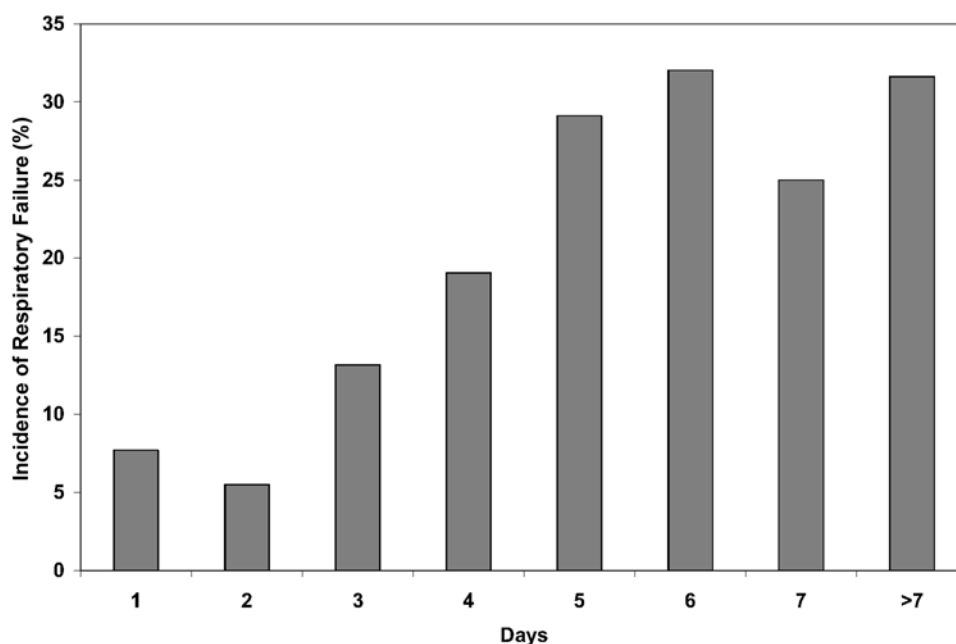


Fig. 1

Incidence of respiratory failure versus time between admission and surgery (in days).

patients in the resulting patient cohort. Patients diagnosed with either acute lung injury or adult respiratory distress syndrome according to this database were considered to have respiratory failure. The criteria for adult respiratory distress syndrome in this database are a PaO₂/FiO₂ (arterial oxygen tension/fraction of inspired oxygen) ratio of <200 and a chest radiograph demonstrating involvement of a minimum of three quadrants. Beginning in 1996, patients with acute lung injury, according to the criteria of a PaO₂/FiO₂ ratio of <300 and a chest radiograph showing involvement of a minimum of three quadrants, were also entered into the registry. The spreadsheets from the trauma registry and the adult respiratory distress syndrome registry were combined into a single spreadsheet for further calculations and statistical analysis with use of the DigDB augmentation software for Microsoft Excel (Data Instrument Group, Mountain View, California).

Statistical Methods

Data were analyzed with use of SAS version-8 software (SAS Institute, Cary, North Carolina). Univariate analysis was performed with use of the two-sample Student *t* test for continuous variables and the chi-square test for categorical variables. Patients with respiratory failure were compared with those without respiratory failure. The time to surgery was considered in terms of the days since admission to the hospital (one to seven days or more) and in terms of whether it was performed on day 1 (from zero to twenty-four hours since admission), day 2 (from twenty-five to forty-eight hours since admission), and so on, and the chi-square test was used to compare the incidence of respiratory failure among the different days. In addition, Pearson correlation coefficients were calculated to determine relationships between continuous

variables, between dichotomous and continuous variables (point-biserial correlation), and between dichotomous variables (phi correlation). The Spearman correlation was calculated between ordinal and continuous variables.

Multiple logistic regression with stepwise selection was performed to identify significant predictors of respiratory failure. Candidate variables were first chosen on the basis of clinical utility. The ISS was initially included as a general indicator of multisystem trauma. The AIS scores were excluded because they were used to calculate the ISS and therefore were not independent of the ISS. Lung contusion and pneumothorax were combined into one variable, blunt lung injury.

We chose variables with a *p* value of <0.2 in the univariate analysis as the final candidates for the logistic model⁶. All continuous candidate variables were converted to categorical variables with two levels. Cutoff points were determined for the ISS, the GCS, and age so that these clinical predictors were outside the 95% confidence intervals derived from the univariate analysis for the patients with and without respiratory failure. The chosen cutoff points were >25 points for the ISS (95% confidence interval, 18.8 to 20.1 points for patients without respiratory failure and 28.1 to 32.2 points for those with respiratory failure), ≤12 points for the GCS (95% confidence interval, 13.3 to 13.7 points for patients without respiratory failure and 7.3 to 9.1 points for those with respiratory failure), and more than thirty-five years for age (95% confidence interval, 32.6 to 34.5 years for patients without respiratory failure and 39.9 to 45.9 years for those with respiratory failure). The cutoff point for the time to surgery was greater than two days after admission and was based on the data presented in Figure 1 and derived with chi-square analysis. The Hosmer-Lemeshow goodness-of-fit test was used to estimate

TABLE I Comparison of Risk Factors Between Patients in Whom Respiratory Failure Developed and Those in Whom It Did Not

Risk Factors	Respiratory Failure* (N = 140)	No Respiratory Failure* (N = 892)	P Value
Patient			
Age (yr)	42.9 ± 17.9	33.5 ± 14.6	<0.0001
Injury			
ISS (points)	30.2 ± 12.4	19.4 ± 9.6	<0.0001
GCS (points)	8.23 ± 5.4	13.54 ± 3.5	<0.0001
Pneumothorax	37 (26.4%)	69 (7.7%)	<0.0001
Lung contusion	43 (30.7%)	61 (6.8%)	<0.0001
Thoracic injury	99 (70.7%)	510 (57.2%)	0.0025
Neurological deficit	51 (36.4%)	264 (29.6%)	0.102
Comorbidity			
Charlson Comorbidity Index Score (points)	0.22 ± 0.52	0.08 ± 0.36	<0.0001
Chronic smoking	7 (5.0%)	56 (6.3%)	0.56
Treatment			
Time to surgery (hr)	132.4 ± 144.5	59.7 ± 87.9	<0.0001
Posterior surgical approach	136 (97.1%)	812 (91.0%)	0.014

*The values are given as the mean and the standard deviation for continuous variables and as the number of patients, with the percentage in parentheses, for categorical variables. The continuous variables were analyzed with use of the two-sample Student t test, and the categorical variables were analyzed with use of the chi-square test.

the regression model fit. A receiver operating characteristic curve was constructed to assess the diagnostic performance of identified predictors. Estimated odds ratios and their 95% confidence intervals were determined with the maximum likelihood method, and the probability of respiratory failure was estimated for each combination of predictors.

Since time to surgery was not allocated randomly, potential selection bias was adjusted for by developing a propensity score^{7,8} for a time to surgery of less than forty-eight hours. Multiple logistic regression with stepwise selection was then used to select variables associated with time to surgery. To improve data match, variables that were removed (because they were not significant) in the stepwise procedure but were clinically relevant to surgical timing were added back to derive a nonparsimonious model. A propensity score was determined for a time to surgery of less than forty-eight hours for each patient by using maximum likelihood logistic regression with the selected variables. The greedy match algorithm⁹ was used to match patients who had undergone surgery less than forty-eight hours after admission (early) with those who had undergone surgery more than forty-eight hours after admission (late). Several variations of this algorithm were attempted, and the one that performed best was chosen. Specifically, we attempted to match a propensity score for each patient who had undergone early surgery to a propensity score that was identical to six digits for a patient who had undergone late surgery. If this could not be done, we attempted a five, four, three, two, or one-digit match. Patients who could not be matched by these criteria were excluded. Logistic regression with stepwise selection was then performed on the matched set, thereby ad-

justing for confounding (potential selection bias).

Results

During the nineteen-year period, 4901 patients with thoracic and lumbar fractures were identified in the trauma registry, and 1209 of these patients had undergone surgical stabilization. The age, date and time of admission to the emergency department, procedure code, and diagnostic code had been recorded for all patients. The time of the procedure was not recorded for 166 patients, 112 of whom were treated before January 1989, when procedure times were not routinely recorded. These 166 patients were excluded. Two patients who did not have an ISS recorded and nine patients who did not have a GCS recorded were excluded as well. Thus, a total of 177 patients were excluded, and the remaining 1032 patients formed the basis of the study. For eight patients, the recorded admission time was after the time that the surgery started, with time differences ranging from 1.25 to 12.37 hours. It was assumed that the admission was administratively recorded after the surgery had started for these patients. For the purposes of the study, the time to surgery was considered to be day 1 of the hospitalization for those patients.

Seventy-nine patients were identified as having coexisting medical conditions. A modified Charlson Comorbidity Index Score was calculated for each patient^{10,11}. The spinal level of injury (thoracic or lumbar) and the presence of a neurological deficit were determined according to the ICD-9-CM diagnostic code that had been entered into the database. Six hundred and nine patients (59%) had thoracic levels of injury and 423 (41%) had lumbar levels of injury. Three hundred and fifteen patients

(31%) had a neurological deficit. The surgical approach was determined from the ICD-9-CM procedure code. When a patient had undergone combined approaches, the surgical approach was considered to be the one used for the primary procedure. Sixty-seven patients underwent both anterior and posterior surgical approaches. Fifty of them had had the posterior surgery initially and a subsequent anterior approach from zero to 221 days later. Seventeen patients had had the anterior surgery initially and subsequent posterior surgery from zero to 205 days later. In total, eighty-four patients (8%) were considered to be have undergone an anterior surgical approach and 948 (92%), a posterior surgical approach. There were sixty-three chronic smokers. One hundred and four patients had a pulmonary contusion, and 106 had a pneumothorax. Forty-nine patients were identified as having acute lung injury and ninety-one, as having adult respiratory distress syndrome; thus, a total of 140 patients had respiratory failure.

An increased time to surgery correlated significantly ($p < 0.001$) but not strongly with the Charlson Comorbidity Index Score ($r = 0.13$), AIS head score ($r = 0.23$), AIS chest score ($r = 0.03$), ISS ($r = 0.18$), GCS ($r = -0.28$), age ($r = 0.13$), and blunt lung injury ($r = 0.16$), indicating a tendency for surgical delay in some patients. Also, there were significant changes from 1989 to 2004. As only four patients were enrolled in 2004, that year was excluded from the trend analysis. The number of patients enrolled each year increased from thirty-one in 1989 to eighty-six in 2003 ($r = 0.84$, $p < 0.0001$). The mean time to the operation decreased significantly from four to two days ($r = -0.56$, $p = 0.03$). There was a significant increase ($r = 0.82$, $p = 0.0002$) in the incidence of adult respiratory distress syndrome, from 6% to 13%. The increase in adult respiratory distress syndrome was associated with a sig-

nificant increase in the ISS ($r = 0.62$, $p = 0.0126$) and a significant decrease in the GCS ($r = -0.79$, $p = 0.0004$). Therefore, over the fourteen-year period covered by this study a greater number of patients were operated on each year and the incidence of adult respiratory distress syndrome increased as the severity of the injuries apparently increased.

The incidence of respiratory failure versus the time to surgery was determined (Fig. 1). No significant difference in the incidence of respiratory failure was detected between day 1 and day 2 ($p = 0.32$), whereas a marginal increase was detected between day 2 and day 3 ($p = 0.05$). There was a significant difference in the incidence of respiratory failure between day ≤ 2 and day > 2 ($p < 0.0001$), indicating that a delay in surgery of more than two days significantly increased the chance of respiratory failure. Patients with respiratory failure differed significantly from those without respiratory failure ($p < 0.05$) with regard to age, ISS, incidence of pneumothorax, incidence of pulmonary contusion, Charlson Comorbidity Index Score, level of spinal injury (thoracic versus lumbar), surgical approach (anterior versus posterior), GCS, and time to surgery (in hours) (Table I). All of the five AIS scores except the AIS abdomen score ($p = 0.8$) were significantly associated with respiratory failure ($p < 0.05$). Respiratory failure was positively correlated with both duration of hospitalization ($r = 0.47$, $p \leq 0.0001$) and duration of the stay in the intensive care unit ($r = 0.60$, $p \leq 0.0001$). There were twenty-three deaths during hospitalization, and death during hospitalization was positively correlated with respiratory failure ($r = 0.2$, $p < 0.0001$).

We identified five important predictors of respiratory failure (Table II): age, ISS, GCS, blunt lung injury, and time to surgery. The ISS was dropped from the model, on the basis of both practical and statistical considerations, in order to derive

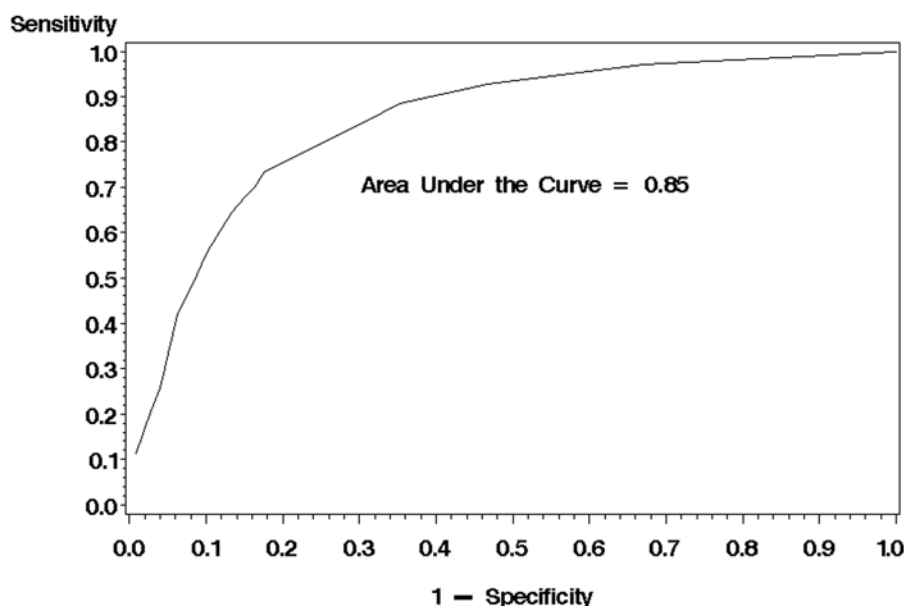


Fig. 2

Receiver operating characteristic curve for a model predicting respiratory failure without consideration of the Injury Severity Score.

TABLE II Significant Predictors of Respiratory Failure Determined by Logistic Regression with Stepwise Selection

Multivariate Predictor	Regression Coefficient	P Value	Odds Ratio Point Estimate	95% Wald Confidence Interval
Intercept	-4.2	<0.0001		
Age >35 yr	0.8	<0.0001	2.3	1.5-3.6
ISS >25 points	0.8	0.0003	2.2	1.4-3.4
GCS ≤12 points	1.6	<0.0001	4.9	3.1-7.6
Blunt lung injury	1.1	<0.0001	3.0	2.0-4.7
Time to surgery >2 days	1.1	<0.0001	2.9	1.9-4.4

a more parsimonious model. The ISS is typically formally calculated, for entry into the trauma registry, at the conclusion of the hospitalization and not during the initial clinical evaluation. Furthermore, the regression coefficient and p value for the logistic regression with stepwise selection indicated that the ISS is the least predictive variable among the significant predictors. The Hosmer-Lemeshow goodness-of-fit test revealed no significant departure from good model fit for the model with ($p = 0.20$) or without ($p = 0.22$) the ISS. The area under the receiver operator characteristic curve was 0.86 for the model with the ISS and 0.85 for the model without the ISS (Fig. 2), indicating that the model had a good diagnostic performance with and without the ISS.

The model without the ISS was used to construct an algorithm to determine the predicted probability of respiratory failure based on sixteen possible combinations of the four predictors. This algorithm correlated the relative risk of delaying surgical stabilization for more than two days with risk factors determined at the time of the initial evaluation (Table III).

Propensity analysis yielded a model with a modest ability to differentiate early from late surgery (Hosmer-Lemeshow goodness-of-fit test = 0.4, concordance index = 0.73). Propensity scores, which reflect the probability that a patient would re-

ceive early surgery, ranged from 0.08 to 0.91. It was determined that the greedy four to one-digit-match algorithm performed best for matching patients who had undergone early surgery with those who had undergone late surgery. With use of this algorithm, 301 patients who had undergone surgery within forty-eight hours after admission were matched with 301 patients who had undergone surgery more than forty-eight hours after admission. Univariate analysis revealed no significant differences between the propensity matched patients ($n = 602$) with regard to any of the variables (all $p > 0.1$). Logistic regression with stepwise selection of this matched cohort confirmed the findings of the multivariate analysis of the entire cohort of 1032 patients (Table IV). The prediction model based on the matched cohort was only slightly degraded (area under the receiver operator characteristic curve = 0.826, Hosmer-Lemeshow goodness-of-fit test = 0.14) compared with the model based on the entire (unmatched) cohort of 1032 patients (area under the receiver operator characteristic curve = 0.85, Hosmer-Lemeshow goodness-of-fit test = 0.28).

Discussion

Initial stabilization of long-bone fractures in multiply injured patients is now the preferred course of action in many

TABLE III Distribution of Predictors Present at Initial Evaluation and Simplified Algorithm for Predicting Probability of Respiratory Failure Depending on Surgical Timing

GCS ≤12 Points	Age >35 Yr	Blunt Lung Injury	Predicted Probability of Respiratory Failure (Relative Risk*)	
			Surgery ≤2 Days after Admission	Surgery >2 Days after Admission
No	No	No	0.021 (1)	0.062 (3.0)
No	Yes	No	0.048 (2.3)	0.13 (6.2)
No	No	Yes	0.072 (3.4)	0.19 (9.0)
Yes	No	No	0.11 (5.2)	0.28 (13.3)
No	Yes	Yes	0.15 (7.1)	0.36 (17.1)
Yes	Yes	No	0.23 (11.0)	0.47 (22.4)
Yes	No	Yes	0.31 (14.8)	0.58 (27.6)
Yes	Yes	Yes	0.51 (24.3)	0.76 (36.2)

*Risk relative to probability of respiratory failure in the absence of any identified risk factors is given in parentheses.

TABLE IV Multivariate Analysis of Patients Matched by Propensity Scores

Variable	P Value	Odds Ratio Point Estimate	95% Wald Confidence Limits
Age	0.0002	2.8	1.7-4.9
ISS	0.0013	2.4	1.4-4.2
GCS	<0.0001	4.6	2.6-8.0
Blunt chest injury	0.0005	2.7	1.5-4.7
Time to surgery	<0.0006	2.5	1.5-4.3

trauma centers. Prior to the 1970s, however, the prevailing thought was that early fracture manipulation and stabilization predisposed patients to respiratory deterioration, and the accepted treatment of these injuries was balanced skeletal traction during the acute period and a delay in long-bone stabilization until ten days to two weeks after the injury^{12,13}. In the late 1960s, the wisdom of this approach began to be questioned and, in the early 1970s, the first reports of early long-bone stabilization in multiply injured patients from centers in Europe were published^{14,15}. These studies demonstrated that early mobilization decreases complications of recumbency, including respiratory deterioration, thromboembolic disease, skin breakdown, and disuse atrophy. Early operative stabilization of long-bone fractures, however, continued to be viewed with skepticism by many in the United States¹⁶.

Treatment in the United States began to change in 1985, when Johnson et al., in a retrospective study of 132 multiply injured patients with a femoral fracture, reported that surgical stabilization less than forty-eight hours after the injury decreased the incidence of pulmonary complications¹⁷. Bone et al. subsequently conducted a randomized, prospective study of 178 patients in whom a femoral fracture was treated either within twenty-four hours (early stabilization) or after forty-eight hours (late stabilization)¹⁸. Patients who underwent late stabilization were found to have a higher incidence of pulmonary complications (pneumonia and adult respiratory distress syndrome) and had a longer stay in the intensive care unit and in the hospital. Several other studies¹⁹⁻²¹ confirmed the benefits of early long-bone stabilization, and its role in the care of multiply injured patients became widely accepted.

The utility of surgical stabilization of spinal column injuries continues to be controversial with regard to its effect both on neurological outcome and on the prevention of complications of recumbency. It is recognized that the neurological status associated with most incomplete injuries will improve with either operative or nonoperative care. The ability of surgical decompression to potentiate this improvement is unclear, with some studies of patients demonstrating an apparent improvement in neurological status following surgical decompression and stabilization²²⁻²⁵ and others showing no improvement²⁶⁻²⁸. In addition to the lack of convincing evidence of functional improvement following operative treatment, advocates of nonoperative care have argued that aggressive nonoperative care with rotating beds and thromboprophylaxis yields similar or even

lower morbidity than surgical stabilization²⁹⁻³¹. To our knowledge, the largest study supporting nonoperative care with rotating beds was a retrospective review of 235 patients by Rechtime et al.³². One hundred and seventeen patients were treated with surgical stabilization, and 118 underwent nonoperative care on a kinetic bed for six weeks. There were no significant differences in the incidence of decubitus ulcers, thromboembolic disease, or mortality between the two groups. The surgical group had an 8% incidence of deep infection. Pneumonia developed in only three patients in each group. Forty-eight percent of the surgically treated patients and 56% of the nonoperatively treated patients were noted to have multiple traumatic injuries, although this was not quantitated with use of the ISS or other means and the severity and extent of the other injuries were not reported.

In our current study of a large cohort of patients who had been treated surgically for thoracic and lumbar fractures, multivariate analysis showed operative stabilization of more than two days after admission to be an independent risk factor for the development of respiratory deterioration. This is especially clinically relevant because the other independent risk factors identified in our study—i.e., the GCS, the ISS, age, and blunt chest trauma—are all determined by the circumstances of the injury and are not clinically alterable per se. These other risk factors correlate with the patient's status at the initial evaluation in the emergency room, however, and may be useful for clinical decision-making. Specifically, a GCS of ≤ 12 points indicates the presence of at least a moderate head injury, and an ISS of >25 points correlates in general terms with more severe trauma. These indices possibly also correlate with the magnitude of the inflammatory process that may mediate acute lung injury and adult respiratory distress syndrome both in multiply injured patients^{33,34} and in patients with an isolated traumatic brain injury³⁵. Other studies have also shown the ISS, the GCS, age, and blunt chest trauma to be risk factors for respiratory failure in multiply injured patients³⁶⁻³⁹.

Since surgical timing may be partly under the control of the treating physician, an algorithm to determine the relative risk of delaying operative stabilization in patients with unstable thoracic and lumbar spine fractures was developed. This algorithm predicts that a surgical delay of more than two days results in an increase in the relative risk of respiratory failure ranging from threefold for patients who are less than thirty-five years old and have minimal head trauma and no blunt chest injury to more than thirty-sixfold for patients who are

more than thirty-five years old and have serious head trauma and a blunt chest injury. The obvious question is whether surgery was delayed a priori for patients with serious head and/or chest injuries. Pearson correlation analysis demonstrated that surgical delay had a modest correlation with the AIS head score and the GCS and lesser correlations with blunt lung injury, age, the ISS, the AIS chest score, and the Charlson Comorbidity Index Score. In spite of these correlations, however, surgical delay was found to be an independent risk factor for respiratory failure in a multivariate analysis of the cohort matched by propensity analysis. The surgical approach, another variable that depends on clinical decision-making, was not an independent risk factor for respiratory failure in our population. The large predominance of posterior surgery (92%) in this series of patients reflects an institutional bias, and it is possible that the surgical approach would be demonstrated to be an independent risk factor in a population with a more equitable distribution of surgical approaches.

This study has several weaknesses. Limitations of the data collected in the trauma registry prevented examination of other factors that are known to influence the risk of respiratory failure, such as a history of blood transfusion, hypotension at the time of the initial presentation, and metabolic acidosis. In addition, the time to surgery was determined from the time of admission, not the time of injury, because the time of injury is frequently not recorded in the trauma registry. Finally, clinical interventions such as the use of rotating beds could not be evaluated. We share the concerns that many have expressed about the quality of data in a large administrative database and its adequacy for use in an outcomes study. Some variables, such as age, the ISS, the types of traumatic injuries, and the types of surgical procedures, are mandatory entries into the trauma registry (which is audited on a quarterly basis at the state registry level) and therefore their documentation is presumably more accurate than entries such as comorbidities and smoking history, which are not directly trauma-related. Medical comorbidities and smoking history were, most likely, largely underreported in our database, and this limited our analysis of these variables. In particular, the 6.1% incidence of smoking identified in our cohort of patients is far below the current incidence of smokers in the United States population, which is 22.5%⁴⁰.

Within the limitations of this study, it appears that the in-

cidence of respiratory failure in multiply injured patients undergoing operative stabilization of thoracic and lumbar spine fractures is decreased if the surgery is performed within two days after admission. Optimal treatment of these patients is complex and requires multidisciplinary care coordinated among many health-care providers, including critical care specialists, general surgeons, anesthesiologists, neurosurgeons, orthopaedic surgeons, nurses, and therapists. Surgical timing must be determined for each patient on an individual basis. Future outcomes research with more comprehensive databases, including model validation with a prospectively collected database at our institution, will further define the role and timing of operative stabilization in these patients. ■

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References

- Schlegel J, Bayley J, Yuan H, Fredricksen B. Timing of surgical decompression and fixation of acute spinal fractures. *J Orthop Trauma*. 1996;5:323-30.
- Croce MA, Bee TK, Pritchard E, Miller PR, Fabian TC. Does optimal timing for spine fracture fixation exist? *Ann Surg*. 2001;233:851-8.
- Kerwin AJ, Frykberg ER, Schinco MA, Griffen MM, Murphy T, Tepas JJ. The effect of early spine fixation on non-neurologic outcome. *J Trauma*. 2005;58:15-21.
- West TA, Rivara FP, Cummings P, Jurkovich GJ, Maier RV. Harborview assessment for risk of mortality: an improved measure of injury severity on the basis of ICD-9-CM. *J Trauma*. 2000;49:530-41.
- Treggiari MM, Hudson LD, Martin DP, Weiss NS, Caldwell E, Rubenfeld G. Effect of acute lung injury and acute respiratory distress syndrome on outcome in critically ill trauma patients. *Crit Care Med*. 2004;32:327-31.
- Hoel PG. Introduction to mathematical statistics. 5th ed. New York: Wiley; 1984. p 238-43.
- Joffe MM, Rosenbaum PR. Invited commentary: propensity scores. *Am J Epidemiol*. 1999;150:327-33.
- D'Agostino RB Jr. Propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med*. 1998;17:2265-81.
- Parsons LS. Reducing bias in a propensity score matched-pair sample using greedy matching techniques. Proceedings of the SAS Users Group International Conference; 22-25 April 2001; Long Beach, CA. www2.sas.com/proceedings/sugi26/p214-26.pdf.
- Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis*. 1987;40:373-83.
- Deyo RA, Cherkin DC, Ciol MA. Adapting a clinical comorbidity index for use with ICD-9-CM administrative databases. *J Clin Epidemiol*. 1992;45:613-9.
- Bradford DS, Foster RR, Nossel HL. Coagulation alterations, hypoxemia, and

fat embolism in fracture patients. *J Trauma*. 1970;10:307-21.

13. Renne J, Wuthier R, House E, Cancro JC, Hoaglund FT. Fat macroglobulemia caused by fractures or total hip replacement. *J Bone Joint Surg Am*. 1978;60:613-8.

14. Weller S. [Urgency of osteosyntheses in the first aid for combined injuries]. *Langenbecks Arch Chir*. 1971;329:82-7. German.

15. Riska EB, von Bonsdorff H, Hakkinen S, Jaroma H, Kiviluoto O, Paavilainen T. Primary operative fixation of long bone fractures in patients with multiple injuries. *J Trauma*. 1977;17:111-21.

16. Talucci RC, Manning J, Lampard S, Bach A, Carrico CJ. Early intramedullary nailing of femoral shaft fractures: a cause of fat embolism syndrome. *Am J Surg*. 1983;146:107-11.

17. Johnson KD, Cadambi A, Seibert GB. Incidence of adult respiratory distress syndrome in patients with multiple musculoskeletal injuries: effect of early operative stabilization of fractures. *J Trauma*. 1985;25:375-84.

18. Bone LB, Johnson KD, Weigelt J, Scheinberg R. Early versus delayed stabilization of femoral fractures. A prospective randomized study. *J Bone Joint Surg Am*. 1989;71:336-40.

19. Behrman SW, Fabian TC, Kudsk KA, Taylor JC. Improved outcome with femur fractures: early vs. delayed fixation. *J Trauma*. 1990;30:792-8.

20. Charash WE, Fabian TC, Croce MA. Delayed surgical fixation of femur fractures is a risk factor for pulmonary failure independent of thoracic trauma. *J Trauma*. 1994;37:667-72.

21. Bone JB, McNamara K, Shine B, Border J. Mortality in multiple trauma patients with fractures. *J Trauma*. 1994;37:262-5.

22. Krengel WF 3rd, Anderson PA, Henley MB. Early stabilization and decompression for incomplete paraplegia due to a thoracic-level spinal cord injury. *Spine*. 1993;18:2080-7.

23. Bohlman HH, Freehafer A, Dejak J. The results of treatment of acute injuries of the upper thoracic spine with paralysis. *J Bone Joint Surg Am*. 1985;67:360-9.

24. Bradford DS, Akbarnia BA, Winter RB, Seljeskog EL. Surgical stabilization of fracture and fracture dislocations of the thoracic spine. *Spine*. 1977;2:185-96.

25. McLain RF, Benson DR. Urgent surgical stabilization of spinal fractures in polytrauma patients. *Spine*. 1999;24:1646-54.

26. Flesch JR, Leider LL, Erickson DL, Chou SN, Bradford DS. Harrington instrumentation and spine fusion for unstable fractures and fracture-dislocations of the thoracic and lumbar spine. *J Bone Joint Surg Am*. 1977;59:143-53.

27. McAfee PC, Bohlman HH, Yuan HA. Anterior decompression of traumatic thoracolumbar fractures with incomplete neurological deficit using a retroperitoneal approach. *J Bone Joint Surg Am*. 1985;67:89-104.

28. McKinley W, Meade MA, Kirshblum S, Barnard B. Outcomes of early surgical management versus late or no surgical intervention after acute spinal cord injury. *Arch Phys Med Rehabil*. 2004;85:1818-25.

29. Rechtine GR. Nonsurgical treatment of thoracic and lumbar fractures. *Instr Course Lect*. 1999;48:413-6.

30. Hartman MB, Chrin AM, Rechtine GR. Non-operative treatment of thoracolumbar fractures. *Paraplegia*. 1995;33:73-6.

31. Davies WE, Morris JH, Hill V. An analysis of conservative (non-surgical) management of thoracolumbar fractures and fracture-dislocations with neural damage. *J Bone Joint Surg Am*. 1980;62:1324-8.

32. Rechtine GR 2nd, Cahill D, Chrin AM. Treatment of thoracolumbar trauma: comparison of complications of operative versus nonoperative treatment. *J Spinal Disord*. 1999;12:406-9.

33. Giannoudis PV, Smith RM, Banks RE, Windsor AC, Dickson RA, Guillou PJ. Stimulation of inflammatory markers after blunt trauma. *Br J Surg*. 1998;85:986-90.

34. Pape HC, Giannoudis P, Krettek C. The timing of fracture treatment in polytrauma patients: relevance of damage control orthopedic surgery. *Am J Surg*. 2002;183:622-9.

35. Bratton SL, Davis RL. Acute lung injury in isolated traumatic brain injury. *Neurosurgery*. 1997;40:707-12.

36. Miller PR, Croce MA, Kilgo PD, Scott J, Fabian TC. Acute respiratory distress syndrome in blunt trauma: identification of independent risk factors. *Am Surg*. 2002;68:845-51.

37. Bone LB, Anders MJ, Rohrbacher BJ. Treatment of femoral fractures in the multiply injured patient with thoracic injury. *Clin Orthop Relat Res*. 1998;347:57-61.

38. Crowl AC, Young JS, Kahler DM, Claridge JA, Chrzanowski DS, Pomphrey M. Occult hypoperfusion is associated with increased morbidity in patients undergoing early femur fracture fixation. *J Trauma*. 2000;48:260-7.

39. Waydhas C, Nast-Kolb D, Trupka A, Zettl R, Kick M, Wiesholler J, Schweiberer L, Jochum M. Posttraumatic inflammatory response, secondary operations, and late multiple organ failure. *J Trauma*. 1996;40:624-31.

40. Centers for Disease Control and Prevention. Cigarette smoking among adults—United States, 2002. *MMWR*. 2004;53:427-31.

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